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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,749	06/27/2001	Martin R. Hodge	35800/235887 (5800-19B)	3698

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/894,749	HODGE ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9-2-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-19 are currently pending in this application.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

Examiner notes that applicants have not updated the relationship of the instant application to its parent application that has matured in to a US patent. Examiner urges applicants to amend said information by providing the US patent number in response to this Office action.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants fail to provide appropriate SEQ ID NO to sequences depicted in figures 1-3 either in figures or in the figure descriptions. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 6, 9, 12, 15, 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2, 6, 9, 12, 15, 18 recite the phrase "heterologous amino acid sequences". The metes and bounds of the above phrase is not clear to the Examiner. Specifically it is not clear to the Examiner as to which polypeptides are considered as "heterologous" and to how the said polypeptide is heterologous, i.e., heterologous to the cell expressing SEQ ID NO:2 or 4, or heterologous to the plasmid comprising the nucleotide sequence encoding SEQ ID NO:2 or 4 etc. A perusal of the specification did not provide ample clarification to the Examiner. Correction is required.

Claims 1-4, 6-7, 17-19 are rejected because the invention appears to employ novel vectors and host cells transformed with novel vectors. Since the vectors/host cells are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809. In order for the claims to be enabled, applicants must show that either the plasmids can be made by publicly available materials or that the plasmid as such has been deposited in such a way that it is freely available to the public. The enablement

requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids and the host cells that are transformed using said plasmids.

It appears that applicants have made the deposit in a biological repository. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific plasmid/strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claims 1-4, 6-13, 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide with SEQ ID NO:2 or 4 having RGS

activity (Regulation of G-protein signaling) encoded by polynucleotides with SEQ ID NO:1 or 3, does not reasonably provide enablement for any such polypeptides having 75% identity to SEQ ID NOs:2 or 4 or to the polypeptides encoded by the DNA sequence encoded by cDNA insert of the plasmid with ATCC accession no. 207048, 49 or 50 or any polypeptide having RGS activity and comprising 30 consecutive amino acids of SEQ ID NO:2 or 4 or polypeptides encoded by polynucleotides having 75% sequence identity to SEQ ID NO:1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4, 6-13, 17-19 are so broad as to encompass any polypeptides having 75% identity to SEQ ID NOs:2 or 4 or the polypeptides encoded by the DNA sequence encoded by cDNA insert of the plasmid with ATCC accession no. 207048, 49 or 50 or to any polypeptide having RGS activity and comprising 30 consecutive amino acids of SEQ ID NO:2 or 4 or polypeptides encoded by polynucleotides having 75% sequence identity to SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of RGS polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties,

predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two RGS polypeptides. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO: 2 and 4 as a RGS polypeptide but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polypeptide having 75% identity to SEQ ID NOs:2 or 4 or to the polypeptides encoded by the DNA sequence encoded by cDNA insert of the plasmid with ATCC accession no. 207048, 49 or 50 or any polypeptide having RGS activity and comprising 30 consecutive amino acids of SEQ ID NO:2 or 4 or polypeptides encoded by polynucleotides having 75% sequence identity to SEQ ID NO:1 or 3 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting the RGS activity; (B) the general tolerance of polypeptides with RGS activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on any RGS polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with an enormous number of amino acid modifications to SEQ ID NOS: 2 and 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1(c), 2-3, 8-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polypeptides having RGS activity and comprising any 30 consecutive amino acids of SEQ ID NO:2 or 4. The specification does not contain any disclosure of the structure of all polypeptide sequences included in the claimed genera. The genus of polypeptides claimed is a large variable genus with the potentiality of having many different structures. Therefore, many structurally distinct polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e., that of SEQ ID NO:2 and 4) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus (i.e., comprising a fragment of 30 amino acids of SEQ ID NO:2 or 4) does not constitute a substantial portion of the genus as the remainder of the structure of any polypeptide having RGS activity is completely undefined and the specification does not define the remaining structural features necessary for members of the

genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 11, 14, 17, are rejected under 35 U.S.C. 102(a) as being anticipated by Carninci et al. (EST database accession No. AK036407 and Meth. Enzymol. 1999, Vol. 303, 19-44). This rejection is based upon the public availability of printed publications. Claims 1, 8, 11, 14, 17 of the instant application are drawn to polypeptides having RGS activity and having either 75% sequence identity with SEQ ID NO:2 or 4 or comprising 30 consecutive amino acids of SEQ ID NO:4 or encoded by polynucleotides that are 75% identical to SEQ ID NO:1 or 3. Carninci et al. disclose such a polypeptide that exhibits RGS activity and has more than 75% sequence identity with SEQ ID NO:2 or comprises more than 30 consecutive amino acids of SEQ ID NO:2 or encoded by polynucleotide that is more than 75% identical to SEQ ID NO:1 (see enclosed

sequence alignments along with reference to Carninci reference to Methods in Enzymology). Thus Carninci et al. anticipate claims 1, 8, 11, 14, 17 of this application as written.

Claims 1, 4-5, 8, 11, 14, 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunt et al. (Nature, 1996, Vol. 383(6596):175-177). This rejection is based upon the public availability of a printed publication. Claims 1, 4-5, 8, 11, 14, 17 of the instant application are drawn to polypeptides having RGS activity and having either an amino acid sequence as in SEQ ID NO:2 or 4 or an amino acid sequence that has 75% sequence identity with SEQ ID NO:2 or 4 or comprising 30 consecutive amino acids of SEQ ID NO:2 or 4 or encoded by polynucleotides with SEQ ID NO:1 or 3 or polynucleotides that are 75% identical to SEQ ID NO:1 or 3 or polypeptides encoded by polynucleotides that hybridize to SEQ ID NO:1 or 3 under stringent conditions. Hunt et al. disclose such a polypeptide that exhibits RGS activity which they call as RGS10. The reference however does not disclose the amino acid sequence of the polypeptide or the sequence of the polynucleotide that encodes the same. However, as the polypeptide in the reference and the polypeptide claimed have identical functions or activity, Examiner takes the position that a characteristic such as the amino acid sequence of said polypeptide is an inherent characteristic and that therefore the polypeptide of the reference inherently has an amino acid sequence that is identical to SEQ ID NO:2 or 4 or that the reference polypeptide has at least a 75% sequence identity with SEQ ID NO:2 or 4 or comprises at least 30 consecutive amino acids of SEQ ID NO:2 or 4 or is encoded by polynucleotide with SEQ ID NO:1 or 3 or encoded by polynucleotide that is at least 75% identical to SEQ ID NO:1 or 3 or polynucleotides

that are capable of hybridizing to SEQ ID NO:1 or 3 under said stringent conditions. Thus Hunt et al. anticipate claims 1, 4-5, 8, 11, 14, 17 of this application as written based on inherency.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

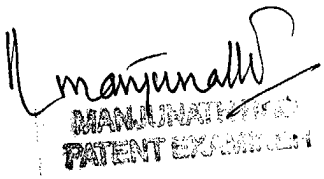
Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
January 9, 2004